## Overview

### Useful For

Follow-up testing to identify mutations in individuals with a clinical diagnosis of cystic fibrosis (CF) and a negative targeted mutation analysis for the common mutations

Identification of mutations in individuals with atypical presentations of CF (eg, congenital bilateral absence of the vas deferens or pancreatitis)

Identification of mutations in individuals where detection rates by targeted mutation analysis are low or unknown for their ethnic background

Identification of patients who may respond to cystic fibrosis transmembrane conductance regulator (CFTR) potentiator therapy

This is **not** the preferred genetic test for carrier screening or initial diagnosis. For these situations, order CFP / Cystic Fibrosis Mutation Analysis, 106-Mutation Panel, Varies

### Genetics Test Information

This test is not the preferred first-tier molecular test for carrier screening or diagnosis. It is used to identify mutations in individuals with a clinical diagnosis of cystic fibrosis (CF) when CFP / Cystic Fibrosis Mutation Analysis, 106-Mutation Panel, Varies is negative or uninformative.

This test includes next-generation sequencing to evaluate for mutations in the CFTR gene. Sanger sequencing may be performed to confirm detected variants.

### Testing Algorithm

See [Cystic Fibrosis Molecular Diagnostic Testing Algorithm](#) in Special Instructions for additional information.

### Special Instructions

- [Molecular Genetics: Congenital Inherited Diseases Patient Information](#)
- [Informed Consent for Genetic Testing](#)
- [Cystic Fibrosis Molecular Diagnostic Testing Algorithm](#)
- [Informed Consent for Genetic Testing (Spanish)](#)

### Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing (when appropriate) and Gene Dosage Analysis by Multiplex Ligation-Dependent Probe Amplification (MLPA)

### NY State Available

Yes

### Specimen

#### Specimen Type

Varies

### Advisory Information
Test Definition: CFTRZ
CFTR Gene, Full Gene Analysis

For first-tier cystic fibrosis molecular testing, order CFP / Cystic Fibrosis Mutation Analysis, 106-Mutation Panel, Varies

Shipping Instructions
Specimen preferred to arrive within 96 hours of collection.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Specimen Type: Whole blood

Container/Tube: Lavender top (EDTA) or yellow top (ACD)

Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

Additional Information:
1. To ensure minimum volume and concentration of DNA is met, the preferred volume of blood must be submitted. Testing may be canceled if DNA requirements are inadequate.

2. Patient education brochures in English (T548) and Spanish (T563) are available upon request.

Forms
1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)

2. Molecular Genetics: Congenital Inherited Diseases Patient Information (T521) in Special Instructions

Specimen Minimum Volume
1 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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Cystic fibrosis (CF), in the classic form, is a severe autosomal recessive disorder characterized by a varied degree of chronic obstructive lung disease and pancreatic enzyme insufficiency. Clinical diagnosis is generally made based on these features, combined with a positive sweat chloride test or positive nasal potential difference. CF can also have an atypical presentation and may manifest as congenital bilateral absence of the vas deferens (CBAVD), chronic idiopathic pancreatitis, bronchiectasis, or chronic rhinosinusitis. Several states have implemented newborn screening for CF, which identifies potentially affected individuals by measuring immunoreactive trypsinogen in a dried blood specimen collected on filter paper.

If a clinical diagnosis of CF has been made, molecular testing for common CF mutations is available. To date, over 1,500 mutations have been described within the CF gene, named cystic fibrosis transmembrane conductance regulator (CFTR). The most common mutation, deltaF508, accounts for approximately 67% of the mutations worldwide and approximately 70% to 75% in the North American Caucasian population. Most of the remaining mutations are rather rare, although some show a relatively higher prevalence in certain ethnic groups or in some atypical presentations of CF, such as isolated CBAVD.

The recommended approach for confirming a CF diagnosis or detecting carrier status begins with molecular tests for the common CF mutations (eg, CFP / Cystic Fibrosis Mutation Analysis, 106-Mutation Panel, Varies). This test, CFTR Gene, Full Gene Analysis, Varies may be ordered if 1 or both disease-causing mutations are not detected by the targeted mutation analysis. Full gene analysis, through sequencing and dosage analysis of the CFTR gene, is utilized to detect private mutations. Together, full gene analysis of the CFTR gene and deletion/duplication analysis identify over 98% of the sequence variants in the coding region and splice junctions.

Of note, FDA guidance has indicated that CFTR potentiator or combination chemical chaperone/potentiator therapies may improve clinical outcomes for patients with a clinical diagnosis of CF and at least 1 copy of a small subset of mutations. If one of the mutations associated with an FDA-approved therapy is identified, this information will be included in the interpretive report.

See Cystic Fibrosis Molecular Diagnostic Testing Algorithm in Special Instructions for additional information.

Reference Values

An interpretive report will be provided.

Interpretation

All detected alterations are evaluated according to American College of Medical Genetics and Genomics (ACMG) recommendations.(1) Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

Cautions

A small percentage of individuals who have a diagnosis of cystic fibrosis (CF) may have a mutation that is not identified by this method (eg, promoter mutations, deep intronic alterations). The absence of a mutation(s), therefore, does not eliminate the possibility of positive carrier status or the diagnosis of CF. For carrier testing, it is important to first document the presence of a cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation in an affected family member.
Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Technical limitations:

In some cases, DNA variants of undetermined significance may be identified.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

In addition to disease-related probes, the multiplex ligation-dependent probe amplification technique utilizes probes localized to other chromosomal regions as internal controls. In certain circumstances, these control probes may detect other diseases or conditions for which this test was not specifically intended. Results of the control probes are not normally reported. However, in cases where clinically relevant information is identified, the ordering physician will be informed of the result and provided with recommendations for any appropriate follow-up testing.

Evaluation tools:

Multiple in-silico evaluation tools were used to assist in the interpretation of these results. These tools are updated regularly; therefore, changes to these algorithms may result in different predictions for a given alteration. Additionally, the predictability of these tools for the determination of pathogenicity is currently unvalidated.

Unless reported or predicted to cause disease, alterations in protein coding genes that do not result in an amino acid substitution are not reported. These and common polymorphisms identified for this patient are available upon request.

Reclassification of Variants-Policy:

All detected alterations are evaluated according to American College of Medical Genetics and Genomics recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance. At this time, it is not standard practice for the laboratory to systematically review likely pathogenic alterations or variants of uncertain significance that have been previously detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Clinical Reference


Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in all coding regions, and intron/exon boundaries of the CFTR gene. Additionally, sequence analysis for genomic regions encompassing select clinically relevant intronic mutations within the CFTR gene is performed, and gene dosage analysis (multiplex ligation-dependent probe amplification) is used to test for the presence of large deletions and duplications in this gene. (Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

14 days

Maximum Laboratory Time

20 days

Specimen Retention Time

Whole Blood: 2 weeks (if available); Extracted DNA: 3 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

81223

81222

LOINC® Information

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